AMENDMENTS

In the Claims:

Please cancel claims 14-21.

Please amend claims 1, 7 and 38 as shown below, and add new claims 39-48:

1. (Three times amended) A method of assaying for risk of developing hereditary lymphedema, comprising assaying nucleic acid of a human subject for a mutation that alters the encoded amino acid sequence of at least one VEGFR-3 allele of the human subject and reduces ligand-mediated signaling of the VEGFR-3 polypeptide encoded by the allele, when compared to VEGFR-3 encoded by a wild-type human VEGFR-3 allele;

and correlating presence or absence of said mutation in the nucleic acid to a risk of developing hereditary lymphedema, wherein presence of said mutation in the nucleic acid correlates with an increased risk of developing hereditary lymphedema, and wherein absence of said mutation in the nucleic acid correlates with no increased risk of developing hereditary lymphedema.

7. (Twice amended) A method of screening for a VEGFR-3 hereditary lymphedema genotype in a human subject, comprising the steps of:

(a) providing a biological sample comprising nucleic acid from said subject, said nucleic acid including sequences corresponding to said subject's VEGFR-3 alleles;

(b) determining a VEGFR-3 genotype by analyzing said nucleic acid for the presence of a mutation altering the encoded amino acid sequence of at least one VEGFR-3 allele, wherein the presence of a mutation altering the encoded amino acid sequence of at least one VEGFR-3 allele of the human subject in a manner that reduces signaling of the VEGFR-3 polypeptide encoded by the allele, when compared to VEGFR-3 encoded by a wild-type human VEGFR-3 allele, identifies a hereditary lymphedema genotype.

38. (Amended) The method of claim 37, wherein said mutation reduces signaling of the VEGFR-3 receptor compared to VEGFR-3 encoded by a wild-type human VEGFR-3 allele.

39. (New) A method according to claim 1, wherein the assaying identifies the presence of the mutation, and the correlating step identifies the increased risk of said patent developing hereditary lymphedema.

40. (New) A method according to claim 2 wherein the assaying identifies a mutation altering a tyrosine kinase domain amino acid sequence of the protein encoded by the VEGFR-3 allele.

41. (New) A method according to claim 3 wherein the assaying identifies the missense mutation in a VEGFR-3 allele in the human subject.

42. (New) A method according to claim 4 wherein the assaying identifies the missense mutation in a VEGFR-3 allele in the human subject.

43. (New) A method according to claim 7 wherein the human subject has a hereditary lymphedema genotype identified by the method of screening.

44. (New) A method according to claim 37 or 38 wherein the human subject has a mutation that alters the encoded amino acid sequence of at least one VEGFR-3 allele in a manner that correlates with the risk of developing hereditary lymphedema.

45. (New) A method according to claim 1, wherein the wildtype VEGFR-3 allele comprises the VEGFR-3 coding sequence set forth in SEQ ID NO: 1.

46. (New) A method according to claim 7, wherein the wildtype VEGFR-3 allele comprises the VEGFR-3 coding sequence set forth in SEQ ID NO: 1.

47. (New) A method according to claim 38, wherein the wildtype VEGFR-3 allele comprises the VEGFR-3 coding sequence set forth in SEQ ID NO: 1.

48. (New) A method of assaying for risk of developing hereditary lymphedema, comprising:

assaying nucleic acid of a human subject for a mutation that alters the encoded amino acid sequence of at least one VEGFR-3 allele of the human subject, relative to the amino acid sequence of VEGFR-3 encoded by SEQ ID NO: 1;

measuring ligand-mediated signaling of the VEGFR-3 polypeptide encoded by the allele of the human subject, relative to ligand-mediated signaling of VEGFR-3 encoded by SEQ ID NO: 1; and

determining risk of developing hereditary lymphedema from the assaying and measuring, wherein presence of a mutation in the nucleic acid that alters the encoded amino acid sequence and reduces ligand-mediated signaling of the encoded VEGFR-3 polypeptide correlates with an increased risk of developing hereditary lymphedema, and wherein absence of said mutation correlates with no increased risk of developing hereditary lymphedema.

REMARKS

I. Restriction Requirement

The Office Action (paragraphs 6-11) requires restriction to one of the following inventions:

Group I: Claims 1-11, 37 and 38 drawn to methods of assaying for the risk of developing hereditary lymphedema;

Group II: Claims 14-17, 20 and 21 drawn to oligonucleotide probes and an array of immobilized oligonucleotide probes

Group III: Claims 18 and 19 drawn to a kit.